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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/757,688	01/11/01	HEIL W	PLOVIN-2A

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EXAMINER	
CHANNAVAJJALA, L	
ART UNIT	**PAPER NUMBER**
1615	11

DATE MAILED: 10/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/757,688	HEIL ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 77-132 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 77-132 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 9
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) [illegible].
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of the following papers is acknowledged:

1. Declaration with power of attorney, dated 6-19-01 (paper # 5)

2. Petition for extension of time and response to notice to file missing parts, dated 6-19-01 (paper #6).

3. Preliminary amendment A, dated 2-23-01 (paper #7)

4. Preliminary amendment B, dated 1-11-01 (paper #8)

5. Supplemental preliminary amendment C, dated 3-29-01 (paper #9) and

6. Information Disclosure Statement, dated 9-25-01 (paper # 10)

Claim Rejections - 35 USC § 112

Claims 77, 86-88, 100-102, 104, 105, 110-114, 116, 122 and 123-132 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 77 recites "first active agent, an estrogen.....second active agent, drospirenone.." It is unclear from the claim recitation if the first active agent comprises estrogen and second agent comprises drospirenone or if the composition contains four active agents namely, first active, estrogen, second agent and drospirenone... From the specification it appears that the first active agent comprises estrogen and second agent comprises drospirenone. Accordingly, appropriate correction is requested.

Claim 86 recites "per cycle". It is unclear to the examiner as to which cycle is being referred to. Clarification is requested.

Claims 104 and 105 recite administering estrogen, a combination of estrogen and drospirenone and placebo in various combinations. However, the claim as recited is not clear as to which step comes after which i.e., is estrogen administered before the combination of estrogen and drospirenone or vice-versa. Further, from the claim language (of claims 104 and 105) it is not clear if estradiol administration is followed by a combination of estradiol and drospirenone or if it is a typographical error that the estradiol is repeated twice in the claim. It is suggested that in order to make the claim clear, the steps of administration are separated by "followed by". A clarification and appropriate correction is requested.

Claim 110 and 111 are vague because the claim only states "continuously", but does not state how long or at least administered as long as required.

Claim 111 states "sequentially" but does not define the sequence of administering drospirenone.

Claim 112 recites the estrogen dosage is "lower", but does not clearly state how much lower and lower than what.

The term "interrupted manner" in claim 113 is vague, as it is not clear as to how administration is interrupted and interrupted by what.

The "3-day-on-3-day-off cycle" stated in claim 114 is vague as it is not clear as to when the cycle starts and ends. For example, in the beginning or mid-way or towards the end of the cycle.

Claim 116 is indefinite because the claim does not state the length of the "treatment-free interval" during the treatment.

In claim 122, the expression "dosage units are administered for 1 to 12 multiples of 28 days" in claim 105 is vague, as it does not clearly express if the dosage units are in multiples or if a single dose is administered for every 28 days in cycles. A clarification and appropriate correction is requested.

Claims 123-132 refer to a multi-phase composition. While the instant specification describes a multi-phase method of administering the composition, there is no definition of a multi-phase composition. Accordingly, the term is indefinite.
A clarification and correction is requested.

Regarding claims 86-88, 100-102, 122, 130 and 131, the phrases "such as", "particularly" and "in particular" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 77-99 are rejected under 35 U.S.C. 102(a) as being anticipated by USPN 5,922,349 to Elliesen et al ('349).

'349 discloses hormone replacement therapy (HRT) method comprising administering estrogen and a progestogen for the treatment of pre-menopausal and menopausal symptoms (col. 1-3, example 1). The estrogen in their composition comprises estradiol and its esters such as valerate, acetate benzoate, and examples of progestogen (drospirenone) (col. 10, lines 1-38). '349 suggest the claimed daily doses of estrogen and drospirenone (DRSP). '349 teach micronized drospirenone. Although, '349 does not specifically mention the protection of endometrium by DRSP in their composition, they teach the same composition as claimed, including the claimed daily ranges. Therefore, the ability to protect endometrium is inherent to the composition of '349. With respect to claim 82, '349 teach the claimed dosages of DRSP, but does not explicitly state the amount per cycle. However, absent evidence on the contrary, the claimed dosage of DRSP is achieved by the method of '349. '349 also teach oral as well as transdermal administration of the composition. '349 do not specifically mention the amounts of drospirenone per cycle. However, absent showing evidence on the contrary, the dosage amount of drospirenone taught by '349 add up to the claimed per cycle amounts.

Claims 77, 81-83, 86-90 and123- 131 are rejected under 35 U.S.C. 102(b) as being anticipated by USPN 5,756,490 ('490, cited on IDS).

'490 disclose compositions and multi-phase packs containing a combination of estrogen and progestogen and estrogen alone, for hormonal contraception. Examiner notes that the instant

claims are directed to compositions. The amounts of DRSP and estradiol disclosed by '490 read on the claimed amounts (see col. 5, lines 45). '490 do not specifically mention the protection of endometrium by DRSP in their composition, they teach the same composition as claimed, including the claimed daily ranges. Therefore, the ability to protect endometrium is inherent to the composition of '490. 490 clearly teach the claimed daily dosage unite, drug-free intervals, the multi-phase packaging units in col. 3, lines 53 through col. 4, lines 38. '490 do not explicitly state the amount per cycle. However, absent evidence on the contrary, the claimed dosage of DRSP is achieved by the method of '490. '490 also teach oral as well as transdermal administration of the composition.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 77-132 are rejected under 35 U.S.C. 103(a) as being unpatentable over 5922349 ('349) by itself or '349 in view of 5,756,490 ('490).

The teachings of '349 and '490 have been discussed above. '349 does not teach each and every condition or symptom associated to with menopause, premenopause and peri-menopause states. However, '349 teach the combination of estrogen and progestogen for hormonoe

replacement therapy in women, so as to prevent the pre-menopausal or menopausal physiological adverse effects, incuding hot flushes, breast tenderness, nausea, menstrual disorders etc. While '349 predominantly teaches transdermal application, the reference suggest oral administration and the dosages suitable for oral administration (col. 10). With reference to the claim limitation, "a multi-phase composition", see the ABOVE 112 REJECTION. Further, '349 teaches a dispenser with separate compartments for estrogen and progestogen, which can also be interpreted as a multi-phase composition. Thus, a multi-phase composition would have been obvious from the kit of '349 because the separation of estrogen and progestogen in the kit allows for administering the two hormones at different doses and different intervals. Furthermore, '349 suggests administering estrogen and progestogen, continuously or sequentially, with a drug-free interval and at various dosages. Accordingly, it would have been within the scope of a skilled artisan at the time of the instant invention to optimize the dosages of estrogen and progestogen, depending on their use together, in a continuous or with-drug free intervals, with an expectation to provide a hormone replacement therapy to prevent or treat any of the effects of menopause, pre- or post-menopause.

Alternatively, '490 teach the same dosages, durations for administration of multi-phase compositions containing estrogen and progestogen. Although, '490 teach for contraception and not menopause, they suggest that separation of estrogen and progestogen as multi-phase compositions for effective administration of estrogen and progestogen, without undesirable side effects. Therefore, it would have been within the scope of a skilled artisan to prepare a multi-phase composition for providing an effective the treatment of disorders associated with estrogen and progestogen imbalance, such as menopause or pre-menopause symptoms.

Claims 77-132 are rejected under 35 U.S.C. 103(a) as being unpatentable over by USPN 5,756,490 ('490, cited on IDS) in view of 5922349 ('349) and Uwe-Hollihn (Essentials Hormone replacement therapy and menopause, submitted on IDS).

'349 and '490 discussed above does not explicitly teach protecting endometrium and the amounts required for protecting endometrium. They also fail to teach instant administration method i.e., the frequency and sequence of administering estrogen and DRSP. However, '349 teaches HRT in women during menopausal and post-menopausal periods to prevents symptoms such as bone loss, structural deformation, the symptoms well known in leading to osteoporosis in menopausal and post-menopausal women. '349 also suggest that a combination of DRSP and estradiol prevent the onset of the adverse effects caused by estrogen administration alone. Accordingly, a skilled artisan at the time of the instant invention would expect that administering DRSP along with estrogen would be able to protect all kinds of adverse effects associated with estrogen treatment, including the effects of estrogen on endometrium.

Further, '349 suggests different regimens in administering the combination of drugs i.e., administering estrogen and DRSP sequentially or together, for different length of time, at different intervals and sequences. Accordingly, optimizing the amounts and steps of administering DRSP and estrogen for HRT would have be within the scope of a skilled because a combination of estrogen and DRSP prevents the adverse effects of estrogen in menopausal women undergoing HRT.

Uwe-Hollihn discusses transition periods from pre-menopause to menopause and post-menopause periods, the hormone imbalance at these periods, the effects of estrogen replacement

on the endometrium and the symptoms and risks associated with it (see pages 27-68, in particular page 48). Further, the reference teaches combination of progestogens with estrogen to reduce endometrial cancer (pages 105-106) and also suggests different regimens of administering i.e., sequential and cyclical administration. Therefore, it would have been obvious for a skilled artisan at the time of the instant invention that, administering the combination of estrogen and DRSP, as suggested by '349 or '490, to menopause women, maintains the estrogen balance as well as prevents the adverse effects of estrogens, especially, endometrial cancer and endometrial atrophy (Uwe-Hollihn).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7921 for regular communications and 703-308-7921 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Lakshmi Channavajjala
October 18, 2001

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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